Remarks/Arguments

Claims 90-96 and 113-125, as amended, are pending for the Examiner's review and reconsideration.

Claims 90, 91, 93, and 94 have been amended for clarity and to correct minor typographical errors. No new matter has been added to the claims by these amendments.

Claims 115 to 125 have been added. Claim 115 is supported by original claim 91. Claims 116 and 117 are supported by original claims 102 to 107, as well as on page 25, lines 5-7 of the specification as filed. Claim 118 is supported on page 17, line 27 to page 18, line 19 of the application as filed. Claims 119 to 121 are supported on page 21, lines 22-31 of the application as filed. Claims 122 and 123 are supported on page 12, line 30 to page 13, line 10 of the application as filed. Claims 124 and 125 are supported on page 12, lines 11-19 of the application as filed. Accordingly, claims 115 to 125 contain no new matter.

Claims 90-96 and 113-114 stand rejected under 35 U.S.C. § 112, first paragraph and 35 U.S.C. § 132 as allegedly containing new matter for the following reasons:

> Claims 90 and 92 recite that the first particles are into the stomach. The specification as filed does not contain a section where the methylphenidate is released from the first and second particles are released into the stomach [sic].

Office Action, p. 3.

Applicants respectfully traverse this rejection. The specification clearly describes dosage forms containing first and second particles of methylphenidate, wherein the first and second particles are released into the stomach. For example, the specification describes a capsule that releases at least two pulses of methylphenidate in the stomach as follows:

> An especially preferred capsule dosage form for pulsed delivery of methylphenidate contains two tablets (reservoirs) containing the drug and coated for timed delay of release. These two tablets are placed in contact with a coated GRDS [gastric retention delivery system] tablet that has...an immediate release dose of methylphenidate as its coating. **When the capsule enters the stomach, the gelatin capsule dissolves,...the immediate dose of methylphenidate is released and the GRDS tablet swells for gastric retention. The three tablet ensemble is retained in the stomach for an extended period. At the predetermined time, e.g. 4 hours, the second dose is released**...

Specification, p. 23, ll. 3-12 (emphasis added).

Further, the specification distinguishes the described dosage forms from those that do

not release the drug in the stomach as follows:

> **The expanding composition of this invention will retain these forms in the stomach until the delay time has passed whereupon the drug will be released in a burst or pulse fashion...Delayed dosage forms that are not coupled to gastric retention will deliver each such dose in a different part of the GI tract** with different absorption profiles for each of the doses. Such therapy would not be equivalent to taking three doses of the drug at the prescribed times, wherein the drug would have been absorbed from the stomach in each case.

Id. at p. 19, l. 31 to p. 20, l. 12 (emphasis added).

For these reasons, the claims are fully supported by the specification and do not contain new matter. Accordingly, the rejection of claims 90-96 and 113-114 under 35 U.S.C. § 112, first paragraph and 35 U.S.C. § 132 as allegedly containing new matter should be withdrawn.

Claims 90-96 and 113-114 also stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. patent No. 6,322,819 ("'819 patent") in view of U.S. patent No. 4,326,525 ("'525 patent") for the reasons set forth on pages 3-5 of the Office Action. In particular, the Office again asserts that the '819 patent discloses a multiple pulsed dose delivery system containing methylphenidate with a disintegration agent and a hydrogel and the '525 patent discloses a dosage form containing methylphenidate and tannic acid. According to the Office, the combination of the delivery system of the '819 patent with the tannic acid disclosed in the '525 patent results in the dosage form recited in the claims. Applicants respectfully traverse.

The claims recite a pharmaceutical dosage form for oral administration to a patient providing pulsed gastric release of methylphenidate comprising a gastric retention vehicle composition comprising about 10 wt-% to about 75 wt-% superdisintegrant, about 2 wt-% to about 12 wt-% tannic acid, and about 20 wt-% to about 70 wt-% of a hydrogel, wherein, upon contact with gastric fluid the gastric retention vehicle composition expands to a sufficient degree such that the dosage form is retained in the stomach and wherein the methylphenidate is released into the stomach in at least two portions.

The disclosure of the '819 patent differs from the recitations of the claims at least in that it does not describe a gastric retention vehicle that expands to promote retention of the dosage form in the patient's stomach in order to accomplish pulsed gastric release of a drug. The '819 patent discloses a pharmaceutical composition that releases a drug in a first portion

in the stomach (immediate release) and a second portion in the small intestine (enteric release). '819 patent, col. 3, ll. 23-38. It does not disclose a gastric retention vehicle that expands to promote retention in the stomach so as to accomplish pulsed release of the drug in at least two portions in the stomach, as recited in the claims. In fact, the '819 patent states that the "desired predetermined area" of release of the second portion is the intestine, and not the stomach. *See id.* at col. 4, ll. 27-31. In addition, the examples of the '819 patent focus on the use of enteric-coated formulations to accomplish the desired release characteristics. *See id.* at col. 10, l. 6 to col. 11, l. 67. Using such enteric coatings, "[t]he pharmaceutical active is not released in the acidic stomach environment of approximately below pH 4.5...[t]he pharmaceutical active should become available when the pH-sensitive [enteric coating] layer dissolves at the greater pH; after a certain delayed time; or after the unit passes through the stomach." *Id.* at col. 8, ll. 14-21. Further, the '819 patent does not disclose the use of tannic acid in a gastric retention vehicle, as recited in the claims.

The '525 patent cannot remedy the above-described deficiencies of the '819 patent because it likewise does not disclose or suggest a gastric retention vehicle having the release characteristics recited in the claims.

The '525 patent discloses an osmotic delivery device that swells to accomplish controlled release, rather than pulsed release, of a drug. '525 patent, col. 2, ll. 40-54. The '525 patent does not teach or suggest that it would be desirable, or even feasible, to accomplish pulsed release of a drug with the disclosed device. By its silence, the '525 patent would not motivate one of ordinary skill in the art to substitute the controlled-release osmotic delivery device of the '525 patent in the pulsed-release formulation of the '819 patent.

Further, even assuming *arguendo* that one of ordinary skill in the art would have been motivated to make such a substitution, he would not have been motivated to make the modifications required to arrive at the claimed invention. He would have to both modify the osmotic delivery device such that it accomplishes pulsed release of a drug and modify the osmotic delivery device such that the pulsed release of the drug is in the stomach in order to arrive at the gastric retention vehicle recited in the claims, without any guidance to make either modification. In fact, in modifying the osmotic delivery device to release the drug in the stomach, one of ordinary skill in the art would have to ignore the express teachings of the '819 patent. The '819 patent teaches that the "desired" area of release of the second portion of the drug is in the intestine, and not the in stomach, as recited in the claims. Neither the '819 patent nor the '525 patent provides any guidance for one of ordinary skill in the art to

choose to ignore this teaching and modify the vehicle such that it releases the second portion of the drug in the stomach. The motivation to modify the vehicle in the manner necessary to arrive at the gastric retention vehicle recited in the claims can only be found in Applicants' disclosure, which has been used by the Office as a blueprint. The Federal Circuit has made it clear that this type of hindsight analysis is an improper standard for obviousness under 35 U.S.C. § 103. *See, e.g., In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988).

Further, the '525 patent discloses the use of tannic acid to increase the solubility of the beneficial agent by its interaction with the beneficial agent in the core of the disclosed device. *Id.* at col. 7, l. 21 to col. 8, l. 47. The claims, however, recite the use of tannic acid as part of the delivery vehicle itself, and not in the core along with the drug. Thus, one of ordinary skill in the art would have to both select tannic acid from among the multitude of buffers disclosed in the '525 patent and choose to remove the tannic acid from the core and place it in the delivery vehicle, without any guidance. Because the '525 patent does not provide any guidance to make these modifications, the '525 patent's disclosure of the use of tannic acid in the core would not motivate one of ordinary skill in the art to modify the composition of the '819 patent to include tannic acid as part of the delivery vehicle, as recited in the claims.

For these reasons, the combined disclosures of the '819 patent and the '525 patent would not motivate one of ordinary skill in the art to arrive at the gastric retention vehicle recited in the claims. Because the Office has failed to meet its burden to make out a *prima facie* case of obviousness in view of these references, Applicants are not required to present evidence that the recited amounts of superdisintegrants, hydrogel, and tannic acid produce a gastric retention vehicle with unexpected properties, as the Office suggests. Office Action, p. 5. Accordingly, the rejection of claims 90-96 and 113-114 as obvious over the '819 patent in view of the '525 patent should be withdrawn.

In view of the foregoing amendments and remarks, Applicants respectfully submit that the present application is in condition for allowance. Early and favorable action by the Examiner is earnestly solicited. If any outstanding issues remain, the examiner is invited to telephone the undersigned at the telephone number indicated below to discuss the same. No fee is believed to be due for the submission of this response. Should any fees be required, please charge such fees to Kenyon & Kenyon, LLP Deposit Account No. 11-0600.

Respectfully Submitted,

Dated: December 4, 2007

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